



4160-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2012-N-0011]

Academic Development of a Training Program for Good Laboratory Practices in High Containment Environments (U24)

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of grant funds for the support of a Funding Opportunity Announcement (FOA) entitled “Academic Development of a Training Program for Good Laboratory Practices in High Containment Environments (U24).” In this FOA, FDA announces its intention to accept and consider a single source application for an award to the University of Texas Medical Branch (UTMB) Galveston National Laboratory (GNL) for the development and implementation of a certified, academic training course for instruction in Good Laboratory Practices (GLP) in a Biosafety Level (BSL) 4 High Containment Environment. FDA seeks to support an effort to design a robust, collaborative, and educational program using problem-based learning techniques designed to bring researchers and regulators together to educate each other on the challenges related to these issues and to identify solutions that are acceptable from both scientific and regulatory perspectives.

DATES: Important dates are as follows:

1. The application due date is July 16, 2012.
2. The anticipated start date is September 15, 2012.

3. The opening date is [INSERT DATE OF PUBLICATION IN THE FEDERAL REGISTER].

4. The expiration date is July 17, 2012.

ADDRESSES: Submit the paper application to: Gladys Melendez Bohler, Office of Acquisitions and Grants Services (HFA-500), 5630 Fishers Lane, rm. 1078, Rockville, MD 20857, 301-827-7175, email: gladys.bohler@fda.hhs.gov. For more information, see section III of the SUPPLEMENTARY INFORMATION section of this notice.

FOR FURTHER INFORMATION CONTACT:

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For more information on this funding opportunity announcement (FOA) and to obtain detailed requirements, please refer to the full FOA located at

<http://www.fda.gov/EmergencyPreparedness/MedicalCountermeasures/default.htm>.

SUPPLEMENTARY INFORMATION:

I. Funding Opportunity Description

Request for Application: RFA-FD-12-024

Catalog of Federal Domestic Assistance: 93.103

A. Background

FDA's Office of Counterterrorism and Emerging Threats (OCET) is a leader and active participant in the public health community and with the military defense community, helping to advance the development, evaluation, and approval of medical countermeasures to be used against threats involving chemical, biological, radiological, or nuclear (CBRN) agents. In 2010, FDA launched its Medical Countermeasures initiative (MCMi) in response to a report by the Secretary of the Department of Health and Human Services to assess the our nation's emergency readiness and in answer to a charge by President Obama to improve our nation's capacity to respond faster and more effectively to CBRN and emerging infectious disease threats--such as

pandemic influenza. OCET was tasked with leading the implementation of the MCMi. OCET's activities are informed by the knowledge that protecting the civilian public and the warfighter against CBRN agents is a national security priority. A significant area of engagement for OCET is its support of innovative science to advance CBRN countermeasure development with the goal of improving access to safe and effective medical countermeasures, should the need arise. These efforts are central to strengthening national preparedness and security.

The "Animal Rule" (21 CFR 314.600 for drugs; 21 CFR 601.9 for biological products) permits animal models to be used to test the effectiveness of a product when testing in humans is neither possible nor feasible. Under the "Animal Rule," pivotal efficacy studies must be conducted in accordance with Good Laboratory Practice (GLP) regulations (21 CFR part 58). Biological threats, such as Ebola virus, Marburg virus, Variola virus, or Lassa fever virus, for which medical countermeasures are needed, require testing in high and maximum biosecurity level (BSL-4) laboratories. These laboratory environments pose daunting challenges to a researcher's ability to meet the requirements of GLP regulations. There has been tremendous progress in the development of candidate interventions over the last decade. However, to date there is not a single facility that is capable of performing pivotal studies under GLP at BSL-4. To break the current choke point in the development process for interventions against agents requiring maximum containment, it will be critical for laboratories with BSL-4 capacity to receive the training and develop the capability necessary to routinely perform pivotal studies in accordance with GLP.

OCET seeks to support an effort to design a robust, collaborative, and educational program using problem-based learning techniques designed to bring researchers and regulators

together to educate each other on the challenges related to these issues and to identify solutions that are acceptable from both scientific and regulatory perspectives.

1. GLP Natural History Studies in BSL-4 Laboratories.

Natural history studies are performed to establish the dose of the disease agent, the route of exposure, and to study the pathogenicity of the disease agent in the animal model. Results of these studies help determine which animal model best describes the disease in humans.

Acceptance of results of these studies for regulatory decision-making is contingent upon these studies being conducted in accordance with GLP. Examples of challenges in meeting GLP requirements include appropriate data recording, record keeping, inspections, and equipment validation. Training on the development of strategies to meet GLP requirements in high and maximum biocontainment laboratories can be realized when everyone has a common understanding of the challenges and requirements. In such a case, the scientific validity and regulatory acceptance of a study can be ensured early on, reducing the need for repeat studies, thereby reducing the numbers of animals needed to address the scientific and regulatory objectives. Once the natural history of the disease in the animal model has been established, it can be used to test the efficacy of antibiotics, vaccine, or other therapies as described in the “Animal Rule.”

2. GLP Animal Efficacy Studies in BSL-4 Laboratories.

Animal efficacy studies are performed in accordance with the “Animal Rule” to test the effectiveness of a medical countermeasure against a specific threat agent in an animal model that best models the disease in humans. Results from these studies also help determine the dose of the medical countermeasure that will be effective in humans. Acceptance of efficacy study results for regulatory decision-making is also contingent upon meeting GLP requirements. To

date, three countermeasure products have been FDA approved using “Animal Rule”-type studies in support of efficacy.

B. Research Objectives

1. The Role of the University of Texas Medical Branch, Galveston National Laboratory

The University of Texas Medical Branch, Galveston National Laboratory (UTMB-GNL) is globally renowned for educational excellence in the sciences, medicine and research, as well as for its Laboratory Biosafety Training Program (LBTP). The LBTP courses are designed to provide training for laboratorians working at BSL-2 through BSL-4 levels. UTMB’s Institutional Office of Regulated Nonclinical Studies (ORNcS) provides oversight for regulated studies and regulatory operations. In addition to the LBTP courses, the ORNcS offers an extensive, high-quality GLP training program to support faculty and staff at UTMB that are conducting nonclinical studies to support product licensure, including nonclinical studies conducted in BSL-3 and BSL-4 laboratories. ORNcS and OCET concur that an educational gap exists regarding the performance challenges of conducting GLP compliant studies in (A)BSL3/4 environments. Both have identified the need for an educational opportunity designed to better link GLP regulatory requirements with BSL-4 laboratory work to increase the efficiency of FDA data review and subsequently facilitate approval of medical countermeasures.

2. Project Description

This project represents a collaborative effort between OCET, the UTMB-GNL, and UTMB ORNcS to support scientific and regulatory collaboration and enhance regulatory science to advance the development of safe and effective antibiotics, vaccines, and other medical countermeasures for use by civilian and military personnel in response to CBRN threat agents. The goal is to develop training strategies for scientists to foster a thorough understanding of the

challenges and establish collaborative classroom environments to find solutions for overcoming hurdles. A common understanding of the challenges and requirements can lead to scientific validity and early regulatory acceptance of a study, reducing the need for repeat studies, thereby reducing the numbers of animals needed to address the scientific and regulatory objectives.

Empowered with knowledge of how to successfully meet GLP requirements in high and maximum biocontainment, scientists working in this environment and FDA staff who will be evaluating applications will be better able to link GLP regulatory requirements with BSL-4 laboratory work, thus increasing the quality of the data and the efficiency of data review, subsequently facilitating approval of medical countermeasures. This project will also lead to improved technical cooperation between FDA and the regulated institutions conducting GLP research in maximum biocontainment. The project has the following goals:

a. Mutual understanding. Progress in the development of animal models for efficacy testing of medical countermeasures has been very slow as developers struggle to design and conduct studies that meet scientific objectives and regulatory requirements for approval. Progress is further slowed as developers are sometimes at a loss with regard to how to satisfy GLP requirements when conducting studies in maximum biocontainment conditions. Currently, FDA's Basic Bioresearch Monitoring training program used to train field inspectors who inspect laboratories for GLP compliance lacks specific guidance for inspection of BSL-3 or BSL-4 laboratories that conduct GLP studies. OCET and ORNcS believe one way to foster progress on this issue is by gathering researchers and regulators together in a nonthreatening educational environment to identify the challenges and needs, then work together to find solutions.

b. Develop collaborations. The training opportunity will bring together the community of researchers involved in conducting research in high and maximum biocontainment

laboratories, who are also interested in conducting “animal rule” studies and animal qualification studies to support medical countermeasure development and approval. In some cases, similar research is being conducted in different laboratories for the same medical countermeasure need. Participants will be encouraged to share experiences and join in collaborations to prevent duplication of research and avoid repetition of failed efforts and otherwise join in support of each other to attain shared goals and facilitate countermeasure development and approval.

3. Continuing Education--Areas of Focus:

- a. GLP in high and maximum containment.--This portion of the training will be a joint UTMB/FDA effort, with UTMB providing the course foundation and FDA offering the field inspector perspective. Lecture examples would include a GLP Refresher, Good Documentation practices, Internal GLP Audits, Equipment Validation and Calibration, and Effective SOPs. Lectures could be followed with practical exercises pointing out specific challenges in meeting GLP requirements that have been encountered in BSL-3 and BSL-4 studies conducted at UTMB.
- b. The “Animal Rule.”--FDA will provide an overview of the regulations for approval of new drugs and biologics based on evidence of effectiveness from studies in animals, including the status of FDA’s draft document entitled, “Guidance for Industry: Animal Models--Essential Elements to Address Efficacy Under the Animal Rule” dated January 2009 (Draft Guidance) and the animal model qualification process.
- c. Animal welfare.--This portion of the training will review animal welfare laws, policies guidelines and requirements, including lectures and discussions on the role of the veterinarian, determination of humane endpoints, and use of supportive care measures in BSL-4 studies.
- d. Telemetry.--Use of telemetry for remote monitoring of routine clinical parameters, such as body temperature, heart rate, respiration rate, and blood pressure is a helpful and

sometimes an essential tool for conducting studies in BSL-4 laboratories. An entire half-day will be devoted to teaching what is available and how to implement telemetry techniques into BSL-4 studies.

4. Dissemination of successful enhancements to the regulatory science and regulation of animal rule studies for medical countermeasure development.

UTMB and OCET will collaborate to incorporate any new FDA guidances and educational tools into the training program as new measures are developed (e.g., drug development tool guidance, updates to GLPs).

C. Eligibility Information

As work in regulatory science for medical countermeasure development progresses, OCET and UTMB anticipate additional collaboration through seminars and training programs, particularly in the areas of GLP in maximum and high biocontainment laboratories, training FDA field inspectors how to effectively conduct GLP inspections in a high or maximum biocontainment laboratories, and training laboratorians and regulators in how to work in high or maximum biocontainment laboratories. With the financial and scientific support from FDA, UTMB is uniquely qualified to undertake these activities, given its mandate as an educational and scientific institution, its high visibility as a pioneer in implementing GLP in maximum and high biocontainment laboratories, and its access to worldwide scientific and regulatory expertise. UTMB has demonstrated a GLP reporting structure and large animal in vivo GLP BSL-4 expertise. In addition, the FDA/UTMB training program will be accessible to researchers at all other university, government, and private organizations.

II. Award Information/Funds Available

A. Award Amount

Only one award will be made.

OCET anticipates providing in FY2012 up to \$150,000 (total costs include direct and indirect costs) for one award subject to availability of funds in support of this project. The possibility of four additional years of support up to \$600,000 of funding is contingent upon successful performance and the availability of funds.

B. Length of Support

The timeframe for this project is 5 years from the award date of the initial application.

III. Paper Application, Registration, and Submission Information:

To submit a paper application in response to this FOA, applicants should first review the full announcement located at

(<http://www.fda.gov/EmergencyPreparedness/MedicalCountermeasures/default.htm>). (FDA has verified the Web site addresses throughout this document, but FDA is not responsible for any subsequent changes to the Web sites after this document publishes in the Federal Register).

Persons interested in applying for a grant may obtain an application at

<http://grants2.nih.gov/grants/funding/phs398/phs398.html>. For all paper application submissions, the following steps are required:

- Step 1: Obtain a Dun and Bradstreet (DUNS) Number
- Step 2: Register With Central Contractor Registration
- Step 3: Register With Electronic Research Administration (eRA) Commons

Steps 1 and 2, in detail, can be found at

http://www07.grants.gov/applicants/organization_registration.jsp. Step 3, in detail, can be found at <https://commons.era.nih.gov/commons/registration/registrationInstructions.jsp>. After you have followed these steps, submit paper applications to: Gladys Melendez Bohler, Office of

Acquisitions and Grants Services (HFA-500), 5630 Fishers Lane, rm. 1078, Rockville, MD
20857.

Dated: June 12, 2012.

Leslie Kux,

Assistant Commissioner for Policy.

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